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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,347	11/14/2003	Joel Richard	017751-042	4071

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
05/08/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/714,347	RICHARD ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-15,17,18 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-15,17,18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/19/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 1/18/08 are acknowledged.

2. Claims 1-2, 4-15, 17-18 and 20 are included in the prosecution.

Continued Examination Under 37 CFR 1.114

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/4/08 has been entered.

Response to Arguments

Rejection of claims 1-13 and 15-20 under 35 USC § 103(a)

4. Applicant's arguments with respect to the rejection of claims 1-13 and 15-20 as being) unpatentable over Jason et al. (US 5,540,927) in view of Guerin et al. (WO 99/38945) have been fully considered but are moot in view of the new ground(s) of rejection.

Claim Objections

5. Claim 1 is objected to because of the following informalities: Claim 1 has steps (a), (b), (c) and (e) but no step (d). Appropriate correction is required.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-2, 4, 7-13, 15, 17-18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yajima et al. JP 05-309261, in view of Gillberg-Laforce et al. (US 5,618,622) and Ezpeleta et al. (International Journal of Pharmaceutics, 131 (1996) 191-200).

The claimed invention is a method for producing microcapsules containing a material to be encapsulated, wherein the method comprises: (a) solubilizing at least one plant protein in an aqueous medium at a pH that is between 2 and 7 to obtain a solution comprising at least one solubilized plant protein; (b) centrifuging the solution of step (a) to obtain a supernatant and a pellet; (c) mixing the supernatant of step (b) with an aqueous solution comprising a polyelectrolyte having the opposite charge of that of the at least one plant protein to obtain a solution comprising at least one solubilized plant protein and a polyelectrolyte having the opposite charge of that of the at least one plant protein; and (e) coacervating the at least one solubilized plant protein and the polyelectrolyte having an opposite charge to the at least one plant protein from the solution of step (c), in the presence of the material to be encapsulated, to form microcapsules comprising a complex coacervate of the plant protein and polyelectrolyte about the material to be encapsulated.

JP 05-309261 teaches the manufacture method of a microcapsule (Detailed Description, [0001]). A polycationic wall material and a polyanionic wall material are subjected to complex coacervation to produce microcapsules (Abstract). The complex coacervation method is disclosed (Detailed Description, [0002]). Wheat gluten extract is used as the poly cation wall membrane material in a microcapsule made by complex coacervation (Detailed Description, [0004]). Polyanion wall materials such as gum arabic, sodium alginate, and agar are disclosed (Detailed Description, [0008]).

JP 05-309261 does not expressly teach cationic polyelectrolytes or the use of glutaraldehyde as a crosslinking agent for hardening the microcapsules.

Gillberg-Laforce teaches polyelectrolytes that include chitosan and sodium carboxymethylcellulose (Col. 4, lines 38-41).

Ezpeleta teaches the formation of nanoparticles from gliadin (a vegetal protein fraction from wheat gluten) (Abstract). Chemical cross-linkage of nanoparticles with glutaraldehyde significantly increased the stability of the gliadin nanoparticles (Abstract). "Nanoparticulate carriers from vegetal macromolecules are a new approach which may present some advantages. Proteins are metabolizable and they can incorporate a wide variety of drugs in a relatively non-specific fashion" (Page 192, right hand column).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a microcapsule with wheat protein extract by complex coacervation, as suggested by JP05309261A, combine it with the polyelectrolytes including chitosan and sodium carboxymethylcellulose, as taught by Gillberg-Laforce,

and the use of glutaraldehyde as a crosslinking agent for gliadin nanoparticles, as taught by Ezpeleta, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Ezpeleta teaches that using plant proteins for producing nanoparticles has advantages of incorporating a wide variety of drugs (Page 192, right hand column). One with ordinary skill in the art would also be motivated to use plant proteins instead of the gelatin that is generally used in complex coacervation for producing microcapsules in order to have a non-animal origin protein source.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the limitation of (step 1a) the method for producing microcapsules comprising solubilizing at least one plant protein would have been obvious over the complex coacervation used to produce gluten microcapsules as taught by JP 05-309261 (Abstract) and by the preparation of gliadin nanoparticles, as taught by Ezpeleta (Page 193, Section 2.2.2). The limitation of the pH of the aqueous medium in which the plant protein is solubilized would have been obvious to one of ordinary skill in the art because during the process of routine experimentation, one would vary the pH of the medium in order to optimize the solubilization of the plant protein. The pH would be varied depending on the plant protein and the solvent chosen. The limitation of (step 1b)

centrifuging the solution would have been obvious over the centrifugation taught by Ezpeleta (Page 193, right hand column). The limitation of (step 1c) mixing the supernatant with a polyelectrolyte having the opposite charge of that of the plant protein would have been obvious over the polyelectrolytes taught by Gillberg-Laforce (Col. 4, lines 38-41). The limitation of (step 1e) coacervating the solubilized plant protein and the polyelectrolyte in the presence of the material to be encapsulated would have been obvious over the complex coacervation used to produce gluten microcapsules as taught by JP 05-309261 (Abstract) and by the preparation of gliadin nanoparticles containing retinoic acid, as taught by Ezpeleta (Page 193, Section 2.2.2).

Regarding instant claim 2, the hardening of the microcapsules after coacervating would have been obvious over the crosslinking of nanoparticles with glutaraldehyde as taught Ezpeleta (Page 193, right hand column).

Regarding instant claim 4, the limitation of adding additional plant proteins to the supernatant would have been obvious over the complex coacervation used to produce gluten microcapsules as taught by JP 05-309261 (Abstract) and by the preparation of gliadin nanoparticles containing retinoic acid, as taught by Ezpeleta (Page 193, Section 2.2.2). During the process of routine optimization, one with ordinary skill in the art would modify the level of plant protein in the supernatant in order to optimize the desired size or thickness of the microcapsules as well as to optimize the stability of the microcapsules with the desired material to be encapsulated.

Regarding instant claims 7-8, the plant protein would have been obvious over the wheat protein used in coacervated microcapsules as taught by JP05309261A (Abstract) and Ezpeleta (Abstract).

Regarding instant claims 9-10, the cationic polyelectrolyte and the anionic polyelectrolyte would have been obvious over the polyelectrolytes chitosan and sodium carboxymethylcellulose, as taught by Gillberg-Laforce (Col. 4, lines 38-41).

Regarding instant claims 11-13, the crosslinking agent would have been obvious over the glutaraldehyde taught by Ezpeleta (Abstract).

Regarding instant claims 15 and 17, the microcapsules would have been obvious over the microcapsules taught by JP05309261A (Abstract) and by Ezpeleta (Abstract).

Regarding instant claims 18 and 20, the limitation of a pharmaceutical composition comprising the microcapsules would have been obvious over the microcapsules comprising retinoic acid as taught by Ezpeleta (Abstract).

8. Claims 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yajima et al. JP 05-309261, in view of Gillberg-Laforce et al. (US 5,618,622), Ezpeleta et al. (International Journal of Pharmaceutics, 131 (1996) 191-200) and Kangas et al. (US 3,843,585).

The teachings of JP05309261A, Gillberg-Laforce and Ezpeleta are stated above.

JP05309261A, Gillberg-Laforce and Ezpeleta do not expressly teach the solubilizing step 1a that is carried out at a pH below the isoelectric pH of the at least one

plant protein, so that the at least one plant protein can be used as a cationic polyelectrolyte in the coacervating step.

Kangas teaches that "the amount of polyelectrolyte combined with the aqueous disperse system is an amount sufficient to coacervate the aqueous disperse system at pH which is below the isoelectric point of the polyelectrolyte and which is above the pH at which the anionizable groups of the disperse material begin to dissociate to form anions" (Col. 8, lines 20-26). "… The coacervated disperse material can be redispersed to a disperse system by adjusting pH of the coacervated system to value above the isoelectric point of the polyelectrolyte prior to curing or film formation of the coacervated disperse material" (Col. 8, line 65 to Col. 9, line 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a microcapsule with wheat protein extract by complex coacervation, as suggested by JP05309261A, combine it with the polyelectrolytes including chitosan and sodium carboxymethylcellulose, as taught by Gillberg-Laforce, and the use of glutaraldehyde as a crosslinking agent for gliadin nanoparticles, as taught by Ezpeleta, further combine it with the aqueous disperse system at a pH which is below the isoelectric point of the polyelectrolyte, as taught by Kangas, and produce the instant invention.

One of ordinary skill in the art would have done this because modifying the pH below the isoelectric pH of the wall material of a coacervated microcapsule is known in the art, as evidenced by the teaching of Kangas.

Regarding instant claim 5, the limitation of carrying out the solubilizing step at a pH below the isoelectric pH of the at least one plant protein would have been obvious over the aqueous disperse system at a pH which is below the isoelectric point of the polyelectrolyte, as taught by Kangas (Col. 8, lines 20-26).

Regarding instant claim 6, the limitation of carrying out the solubilizing step at a pH above the isoelectric pH of the at least one plant protein would have been obvious over the pH adjustment of the coacervated system to a value above the isoelectric point of the polyelectrolyte prior to curing or film formation of the coacervated disperse material" (Col. 8, line 65 to Col. 9, line 2).

9. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yajima et al. JP 05-309261, in view of Gillberg-Laforce et al. (US 5,618,622), Ezpeleta et al. (International Journal of Pharmaceutics, 131 (1996) 191-200) and Lee et al. (Journal of Applied Polymer Science, Vol. 63, Issue 4, 425-432).

The teachings of JP05309261A, Gillberg-Laforce and Ezpeleta are stated above.

JP05309261A, Gillberg-Laforce and Ezpeleta do not expressly teach the use of acetic anhydride as the hardening agent.

Lee teaches hardening microcapsules containing the cationic polyelectrolyte chitosan by using acetic anhydride as the hardening agent (Journal of Applied Polymer Science 1997). Lee teaches that "chitosan, a cationic polysaccharide, was … deacylated … and followed by a homogenous reacylation with acetic anhydrides" (Abstract). It is further taught that polyelectrolyte complexes are formed when chitosan

is complexed with an anionic polysaccharide (like sodium alginate) and drug microencapsulation was the application of the polyelectrolyte complexes produced (Abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a microcapsule with wheat protein extract by complex coacervation, as suggested by JP05309261A, combine it with the polyelectrolytes including chitosan and sodium carboxymethylcellulose, as taught by Gillberg-Laforce, and the use of glutaraldehyde as a crosslinking agent for gliadin nanoparticles, as taught by Ezpeleta, further combine it with the use of acetic anhydride and chitosan, as taught by Lee, and produce the instant invention.

One of ordinary skill in the art would have done this because the addition of acetic anhydride allows the reacylation of chitosan (as taught by Lee), which further cross links or “hardens” the resultant microcapsule.

Regarding instant claim 14, the limitation of chitosan and acetic anhydride would have been obvious over the chitosan and acetic anhydride taught by Lee (Abstract).

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

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